This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF THE CLAIMS

Claim 1 (currently amended): A catalytic DNA molecule having site-specific endonuclease activity specific for a nucleotide sequence defining a cleavage site in a preselected substrate nucleic acid sequence,

said molecule having first and second substrate binding regions flanking a core region,

wherein said first substrate binding region has a sequence complementary to a first portion of said preselected substrate nucleic acid sequence,

said second substrate binding region has a sequence complementary to a second portion of said preselected substrate nucleic acid sequence, and

said core region having a sequence according to the formula:

~~(I.) T(stem)'AGC(stem)"Z,~~

~~wherein said (stem)' and (stem)" are each three sequential nucleotides which when hybridized as a (stem)':(stem)" pair comprise three base pairs including at least two G:C pairs and wherein said Z = WCGR or WCGAA, and W = A or T and R = A or G; or~~

(Formula II[.]) RGGCTAGCHACAACGA (SEQ ID NO 122),

wherein said H = T, C or A, and R = A or G.

Claim 2 (canceled)

Claim 3 (original): The molecule of claim 1 wherein said formula II defines SEQ ID NO 121 (10-23).

Claim 4 (original): The molecule of claim 1 wherein said first or second substrate binding region is from 5 to 13 nucleotides in length.

Claim 5 (original): The catalytic DNA molecule of claim 1 wherein said catalytic DNA molecule comprises deoxyribonucleotides (DNA), modified DNA, nucleotide analogs, or composites thereof.

Claim 6 (original): The catalytic DNA molecule of claim 1 wherein said substrate nucleic acid comprises RNA, DNA, modified RNA, modified DNA, nucleotide analogs, or composites thereof.

Claim 7 (original): The catalytic DNA molecule of claim 1 wherein said catalytic DNA molecule comprises a single-stranded deoxyribonucleic acid having 5' and 3' termini, wherein said termini are modified with exonuclease-resistant nucleotides.

Claim 8 (original): The catalytic DNA molecule of claim 7 wherein said exonuclease-resistant nucleotides comprise nucleoside phosphorothioate.

Claim 9 (original): The catalytic DNA molecule of claim 1 wherein said first or second substrate binding region comprises at least two phosphorothioate nucleosides.

Claim 10 (original): The catalytic DNA molecule of claim 1 wherein said core region comprises a phosphorothioate nucleoside residue on a dipyrimidine within said core.

Claim 11 (original): The catalytic DNA molecule of claim 7 wherein said 3' termini comprises an inverted (3',3'-linked) nucleotide.

Claim 12 (original): The catalytic DNA molecule of claim 1 wherein said catalytic DNA molecule comprises a 2' O-methyl ribonucleotide.

Claim 13 (currently amended): The catalytic DNA molecule of claim 1 wherein said first and second substrate binding regions respectively comprise a nucleotide sequence complementary to a first and a second portion of a sequence selected from the group consisting of SEQ ID NOs 102-119.

Claim 14 (original): The catalytic DNA molecule of claim 1 wherein said molecule catalyzes a reaction with a K_m of about 0.05 - 1000 nanomolar.

Claim 15 (original): The catalytic DNA molecule of claim 1 wherein said catalytic DNA molecule binds said substrate with a K_m of less than about 1.0 micromolar.

Claim 16 (original): The catalytic DNA molecule of claim 1 wherein said catalytic DNA molecule binds said substrate with a K_m of about 0.1 nanomolar.

Claim 17 (original): The catalytic DNA molecule of claim 1 wherein said molecule has a catalytic reaction turnover rate (k_{cat}) of about 0.005 - 0.1 min^{-1}.

Claim 18 (original): The catalytic DNA molecule of claim 1 wherein said endonuclease activity is enhanced by the presence of a divalent cation.

Claim 19 (original): The catalytic DNA molecule of claim 18 wherein said divalent cation is selected from the group consisting of Pb^{2+}, Mg^{2+}, Mn^{2+}, Zn^{2+}, and Ca^{2+}.

Claim 20 (original): The catalytic DNA molecule of claim 18 wherein said endonuclease activity is enhanced by the presence of Mg^{2+}.

Claim 21 (original): The catalytic DNA molecule of claim 1 wherein said endonuclease activity is enhanced by the presence of a monovalent cation.

Claim 22 (original): The catalytic DNA molecule of claim 21, wherein said monovalent cation is selected from the group consisting of Na^{+} and K^{+}.

Claim 23 (withdrawn): A composition comprising two or more populations of catalytic DNA molecules according to claim 1, wherein each population of catalytic DNA molecules is capable of cleaving a different nucleotide sequence in a substrate.

Claim 24 (withdrawn): A composition comprising two or more populations of catalytic DNA molecules according to claim 1, wherein each population of catalytic DNA molecules is capable of recognizing a different substrate.

Claim 25 (original): A method of cleaving a target nucleic acid molecule, comprising:

a) admixing a catalytic DNA molecule according to claim 1 with a target nucleic acid molecule having a preselected substrate nucleic acid sequence to said first and second substrate binding regions, to form a reaction admixture; and

b) maintaining said admixture under predetermined reaction conditions to allow said catalytic DNA molecule to cleave said target nucleic acid molecule, thereby producing a population of substrate products.

Claim 26 (original): The method of claim 25, wherein said substrate comprises RNA.

Claim 27 (original): The method of claim 25, wherein said predetermined reaction conditions include the presence of a monovalent cation, a divalent cation, or both.

Claim 28 (original): The method of claim 25 wherein said admixing comprises introducing said catalytic DNA molecule into a cell containing said target nucleic acid molecule.

Claim 29 (currently amended): A method of engineering a catalytic DNA molecule that cleaves a preselected substrate nucleic acid sequence in a target nucleic acid molecule, comprising the steps of:

a) selecting a substrate nucleic acid sequence of from 10 to 26 nucleotides in length in a target nucleic acid molecule; and

b) synthesizing a deoxyribonucleic acid molecule comprising first and second substrate binding regions flanking a core region,

wherein said first substrate binding region has a sequence complementary to a first portion of said preselected nucleic acid target sequence,

said second substrate binding region has a sequence complementary to a second portion of said preselected nucleic acid target sequence, and

said core region having a sequence according to the formula:

~~(I.) T(stem)'AGC(stem)"Z,~~

~~wherein said (stem)' and (stem)" are each three sequential nucleotides which when hybridized as a (stem)':(stem)" pair comprise three base pairs including at least two G:C pairs and~~

~~wherein said Z = WCGR or WCGAA, and W = A or T and R = A or G; or~~

(Formula II[.]) RGGCTAGCHACAACGA (SEQ ID NO 122), wherein said H = T, C or A, and R = A or G.

Claim 30 (canceled)

Claim 31 (original): The method of claim 29 wherein said formula II defines SEQ ID NO 121 (10-23).

Claim 32 (original): The method of claim 29 wherein said first or second substrate binding region is from 5 to 13 nucleotides in length.

Claim 33 (original): The method of claim 29 wherein said catalytic DNA molecule comprises deoxyribonucleotides (DNA), modified DNA, nucleotide analogs, or composites thereof.

Claim 34 (original): The method of claim 29 wherein said catalytic DNA molecule comprises a single-stranded deoxyribonucleic acid having 5' and 3' termini, wherein said termini are modified with exonuclease-resistant nucleotides.

Claim 35 (previously presented): The method of claim 34 wherein said exonuclease-resistant nucleotides comprise nucleoside phosphorothioate.

Claim 36 (original): The method of claim 29 wherein said first or second substrate binding region comprises at least two phosphorothioate nucleosides.

Claim 37 (original:) The method of claim 29 wherein said

core region comprises a phosphorothioate nucleoside residue on a dipyrimidine within said core.

Claim 38 (original): The method of claim 34 wherein said 3' termini comprises an inverted (3',3'-linked) nucleotide.

Claim 39 (original): The method of claim 29 wherein said catalytic DNA molecule comprises a 2' O-methyl ribonucleotide.

Claim 40 (currently amended): The method of claim 29 wherein said first and second substrate binding regions respectively comprise a nucleotide sequence complementary to a first and a second portion of a sequence selected from the group consisting of SEQ ID NOs 102-119.

Claim 41 (original): The method of claim 29 wherein said molecule catalyzes a reaction with a K_m of about 0.05 - 1000 nanomolar.

Claim 42 (original): The method of claim 29 wherein said molecule has a catalytic reaction turnover rate (k_{cat}) of about 0.005 - 0.1 min^{-1}.

Claim 43 (original): The method of claim 29 wherein said endonuclease activity is enhanced by the presence of a divalent cation.

Claim 44 (original): The method of claim 43 wherein said divalent cation is selected from the group consisting of Pb^{2+}, Mg^{2+}, Mn^{2+}, Zn^{2+}, and Ca^{2+}.

Claim 45 (original): The method of claim 29 wherein said endonuclease activity is enhanced by the presence of a monovalent

cation.

Claim 46 (original): The method of claim 45, wherein said monovalent cation is selected from the group consisting of Na^+ and K^+.

Claim 47 (new): The method of claim 29 wherein said substrate nucleic acid comprises RNA, DNA, modified RNA, modified DNA, nucleotide analogs, or composites thereof.

Claim 48 (new): The method of claim 29 wherein said catalytic DNA molecule binds said substrate with a K_m of less than about 1.0 micromolar.

Claim 49 (new): The method of claim 29 wherein said catalytic DNA molecule binds said substrate with a K_m of about 0.1 nanomolar.

Claim 50 (new): The method of claim 43 wherein said endonuclease activity is enhanced by the presence of Mg^{2+}.